

## **ATTACHMENT A**

### **REMARKS**

Claims 1-35 stand pending in the present application. By this Amendment, Applicants have amended claims 1-6, 8 and 10-26, added new claims 27-35 and canceled claims 7 and 9. Applicants respectfully submit that the present application is in condition for allowance based on the discussion below.

Claims 1-26 were rejected under 35 U.S.C. § 112, second paragraph. Claims 1-23 were also objected to for failing to clearly separate the steps of the recited process. By this Amendment, Applicants have amended the claims to further clarify the recited invention and to put the claims in a more conventional U.S. claim form. Further, Applicants have added new claims 27-35 directed to previously recited preferred embodiments recited in the prior dependent claims.

Specifically, the term “functionalized” in claim 12 has been clarified by reciting that such functionalization comprises succinylation, methylation, grafting of fatty acids or any other method to modify collagen.

With respect to claim 21 (currently amended), the term “highly” has been omitted. Further, the wording of claim 21 has also been clarified to more particularly point out the process steps. Similarly, the wording of claim 23 has been clarified by separating the process steps.

In claim 24, the wording has been amended so as to clarify that the first layer is formed from a crosslinked collagenic component, whereas the second layer is formed of a crosslinked collagen fibers.

In claim 25, the antecedent basis for “wet state” has been clarified. Additionally, the term “network” has been omitted, so as to avoid any ambiguous antecedent basis in claim 24.

The steps of the process in the process claims have been clearly separated by a line indentation as required in the Office Action.

Based on the foregoing discussion, Applicants respectfully request that the 35 U.S.C. § 112, second paragraph, rejection to the claims be withdrawn.

Claims 1 and 3-23 were rejected under the judicially created doctrine of double patenting over claims 19-39 of U.S. Patent No. 6,391,939 (hereinafter the ‘939 patent).

Applicants respectfully submit that the present claims are distinct from the ‘939 patent and are novel over the claims in the ‘939 patent as well as being novel and not obvious over the combination of the ‘939 patent in view of U.S. Patent No. 3,808,113 (hereinafter the ‘113 patent).

With regard to claims 19-39 of the ‘939 patent, the ‘939 patent claims fail to teach or suggest irradiating a collagenic component in a wet state with beta radiation. On the contrary, the ‘939 patent clearly teaches the use of a dried film which contains residual water up to 20% and typically around 8% (the ‘939 patent, column 8, line 55). Further distinctions between the presently claimed invention and that of the ‘939 patent and the ‘113 patent will be discussed below with regard to the 35 U.S.C. § 103(a) rejection to the present claims. Based on the foregoing discussion, Applicants respectfully request that the double patenting rejection to the claims be withdrawn.

Claims 24 and 26 were rejected under 35 U.S.C. § 102(b) as being anticipated by Carr et al (U.S. Patent No. 5,733,337, hereinafter “Carr”).

Contrary to the Examiner's allegation, claims 24-26 are not anticipated by Carr as Carr fails to teach irradiation of collagen in the wet state as claimed. Moreover, Carr actually suggests the irradiation of the prosthetic device in a dry state (see Carr, column 6, lines 53-55). Accordingly, the disclosure of Carr is dramatically different from the present invention.

Furthermore, according to the presently amended claims, the collagenic component comprises collagen that has at least partially lost its helical structure by heating the collagen above 37°C. Consequently, the presently claimed invention is based on the use of denatured collagen.

In sharp contrast to the present invention, Carr teaches the use of collagenous tissue from a mammalian body (see Carr, column 2, line 63) which necessarily means that the collagenous tissue is not denatured by the application of heat (see Carr, column 3, lines 50-54). And, in fact, Carr actually uses collagenous tissues which are naturally fibrous where the naturally occurring collagen can be heated up to 70°C without denaturing the collagen (see Carr, column 3, line 61).

Contrary to the disclosure of Carr, the present invention uses extracted collagen which is denatured by heating to a temperature above 30°C (see present specification, page 8, line 25). Consequently, the collagen used by Carr is not denatured and differs substantially from the collagen according to the present invention which is necessarily denatured. As a result, the collagenic bicomposite claimed in claims 24-26 of the present application is inherently different from that disclosed in Carr.

Based on the foregoing discussion, Applicants respectfully request that the rejection to claims 24-26 as being anticipated under 35 U.S.C. § 102(b) by Carr be withdrawn.

Claims 1 and 3-23 were rejected under 35 U.S.C. § 102(e) as being anticipated by the '939 patent. Contrary to the Examiner's allegation, as described above, the '939 patent is specifically directed to the preparation of dry films and thus fails to provide an enabling disclosure which teaches, let alone suggests, beta irradiation of a collagenic component in a wet state. On the contrary, the '939 patent specifically discloses the preparation of exclusively dried films. For example, in the '939 patent, column 8, lines 51-52, the patent teaches that the dried film should contain residual water up to 20% and typically 8% (the '939 patent, column 8, line 55). Moreover, the '939 patent is completely silent with respect to collagen in a wet state. Consequently, the disclosure of the '939 patent with respect to wet collagen is in no way enabling.

Furthermore, Applicants respectfully submit that the collagen disclosed in the '939 patent is inherently different from the collagen of the present invention. Namely, the present specification comprises a comparative example based on collagen described in the '939 patent (see present specification, pages 23-24). According to this comparative example, the collagen produced by the '939 patent is submitted to beta and gamma irradiation. The dried film irradiated by gamma rays is more crosslinked, whereas the material irradiated by beta rays dissolves quickly. By contrast, the collagen in the wet state according to the present invention is highly reticulated when irradiated by beta radiation, whereas, when irradiated by gamma rays, such collagen in wet state dissolves.

Consequently, the process of the present invention comprising irradiation by beta radiation results in crosslinked collagen, whereas the process disclosed in the '939 patent, when comprising irradiation by beta radiation, leads to degradation of the material. Consequently, the two processes are completely opposite. As a result, claims 1 and 3-23 are novel over the disclosure of the '939 patent.

In view of the foregoing discussion, Applicants respectfully submit that claims 1 and 3-23 are not anticipated by the '939 patent under 35 U.S.C. § 102(e) and accordingly respectfully request that the Examiner withdraw the rejection to the aforementioned claims.

Claims 1 and 2 were rejected under 35 U.S.C. § 103(a) as being unpatentable over the '939 patent in view of the '113 patent.

The present invention is not obvious from the '939 patent in view of the '113 patent for at least reciting the irradiation of collagen in a wet state by beta radiation which is not taught nor suggested in the individual or *arguendo* combined references.

The present claims are directed to a process comprising irradiation of collagen in the wet state by beta radiation in which the collagen has at least partially lost its helical structure by heating above 37°C. According to the claimed process, irradiation by beta radiation of collagen in the wet state is crosslinked. By contrast, the same collagen irradiated by gamma rays dissolves easily.

The '939 patent teaches that dry collagen irradiated by beta radiation dissolves easily, whereas irradiation by gamma rays of dried collagen leads to crosslinking. Consequently, the '939 patent teaches the opposite effect of irradiation on dried material.

However, the '113 patent teaches that electron beam (that is, beta radiation) or gamma rays (radioactive rays) do have the same effect, that is, crosslinking, on wet collagen. This is dramatically different from the present invention. This is because, in fact, the '113 patent uses a different collagen as that used according to the present invention. Namely, the '113 patent teaches that the collagen should not be denatured and, as a result, should not be heated above 30° to 37°C (see the '113 patent, column 4, lines 57-62). Consequently, the '113 patent does not disclose irradiation by beta radiation of wet collagen, which has at least partially its helical structure by heating above 37°C.

In view of the '113 patent, a person of ordinary skill in the art seeking to obtain crosslinked collagen would have irradiated undenatured collagen by beta or gamma rays. The artisan would not have been motivated to carry out this irradiation on denatured collagen, as in the present invention.

In fact, the '113 patent teaches away from the present invention, dissuading the artisan from irradiating collagen with beta radiation in which the collagen has at least partially lost its helical structure by heating above 37°C. The skilled person, seeking to crosslink collagenic material, would not have combined irradiation in the wet state with denatured collagen. As a result, the teaching of the '113 patent would not have been combined with the '939 patent for this purpose.

Based on the foregoing discussion, Applicants respectfully submit that the present claims are novel and not anticipated by the '939 patent individually or combined with the '113 patent. Therefore, Applicants respectfully request that the rejection to

claims 1-2 under 35 U.S.C. § 103(a) as being unpatentable over the '939 patent in view of the '113 patent be withdrawn.

Based on the foregoing discussion, Applicants respectfully submit that the present application is now in condition for immediate allowance.

**END REMARKS**